REMARKS

Entry of this amendment is respectfully requested.

The present invention relates to a new class of substituted 4-6, 6- or 7-hyroxyindoles having a pyridine-N-oxide-group which are inhibitors of phosphodiesterase 4 (PDE4) activity as well as to their use as medicaments. PDE4 inhibitor compounds of the prior art at the time of the invention showed several disadvantages such as various side effects, e.g. nausea and emesis. Therefore, there was a need for novel PDE4 inhibitors with improved therapeutic index.

It is an object of the invention to provide compounds which are effective as PDE4 inhibitors in the treatment of diseases which are associated with PDE4 activity. According to the invention, this object was achieved by a compound having the claimed substitution pattern.

Höfgen I is regarded as closest reference. Höfgen I describes 5-hydroxyindoles with a N-oxide group and their use in the inhibition of phosphodiesterase 4 activity, in particular in immunocompetent cells. However, the compounds of Höfgen I differ from the claimed compounds in that they are substituted obligately at the 5 position of the indole ring with an OH-group, wherein the inventive compounds are substituted at the 4, 6 or 7 position of the indole ring with at least one OH-group.

Based on the disclosure of Höfgen II and III, it is submitted that a person skilled in the art could not have arrived at the present invention by combining Hofgen II and/or III with Höfgen I, since neither of Höfgen II and III do not give any hint or suggestion to use a compound having a pyridine-N-oxide-group.

Höfgen II and III disclose compounds which can be used as inhibitors of phosphodiesterase 4. They have a similar structure to the compounds according to the invention, but in contrast, as already mentioned, they do not have a pyridine-N-oxide-group. Further, the specific substitution pattern at the phenyl ring of the indole ring is also not disclosed in Höfgen II and III. There is no hint or suggestion Höfgen II and III to combine the N-oxide of the pyridine ring with the specific substitution pattern at the phenyl ring of the indole ring.

Therefore, a person skilled in the art is not motivated by Höfgen II and/or III to combine it with Höfgen I in order to arrive at the subject matter of the present invention.

Gunther disclose substituted N-benzyl-indol-3-yglyoxylic acid derivatives which can be substituted with a pyridine-N-oxide-group at the nitrogen of the amide; the compounds, however do not have a hydroxy-group at the indole ring. Gunther desires a totally different medical indication, namely an anti-tumor action. Further, there is no hint or suggestion in Gunther that the compounds can be used as inhibitors of PDE4.

Therefore, as neither the claimed compounds nor the object of the invention is mentioned in Gunther, a person skilled in the art would not have combined Höfgen I-III with Günter in order to arrive at novel PDE4 inhibitors in accordance with the invention.

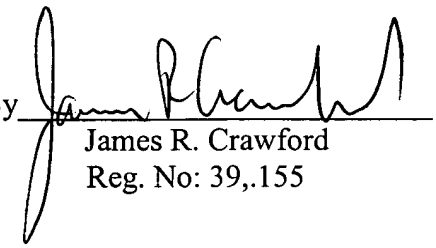
In sum, a person skilled in the art could not have gathered any hint or suggestion from the cited references concerning the subject matter of the present invention, neither alone nor in combination. Therefore, presently pending claims 1-6 and 14 are believed to be allowable over the cited references.

Enclosed is a verified English translation of the German priority document which is believed to overcome the 35 U.S.C. § 103(a) and the obviousness-type double patenting rejections of claims by antedating certain cited references.

The Commissioner is hereby authorized to charge any deficiency in the fees filed to our Deposit Account No. 50-0624, under Order No. NY-HUBR 1262-US.

Respectfully submitted

FULBRIGHT & JAWORSKI L.L.P.

By 

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Enclosure